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The University of Toronto Medical Journal

VOL. IV APRIL, 1927 NO. 6

EDITORIAL.

THE SCHOOL OF HYGIENE.

The School of Hygiene, University of Toronto, was established in 1925. In 1924 the International Health Board of the Rockefeller Foundation made a contribution of $650,000 to the Governors of the University of Toronto for the purpose of assisting in the creation of the school. Of this sum, approximately $400,000 was given to provide this building and the balance, namely, $250,000, was donated for the purpose of endowment.

The School of Hygiene will provide accommodation for the Department of Hygiene and Preventive Medicine and Public Health Nursing, and in addition will house a part of the public service section of the Connaught Laboratories as well as the research division of those Laboratories. The work of research in the School of Hygiene will be co-ordinated with that conducted in the Connaught Laboratories.

The School of Hygiene will thus in the future house those departments of the University responsible for graduate and undergraduate teaching in Hygiene, Preventive Medicine and Public Health.

In this building, also, a somewhat novel undertaking will be carried on in which the three functions of research, teaching and public service will be prosecuted by members of the University staff in the subjects already mentioned. Provision has been made for the organization of sections of Biometrics and Epidemiology and Physiological Hygiene in this School. Research and teaching in those subjects will be carried on. Quarters have also been provided where the administrative work of the Insulin Committee, University of Toronto, may be undertaken.

Introductory Address.

On the Occasion of His First Lecture to 2T7

By MR. I. H. CAMERON

Ladies and Gentlemen of the Final Year.

I am much indebted to the courtesy of my old colleagues of the Faculty of Medicine and to the complacency of the Board of Governors which have conspired together to give me the opportunity (a final one, while I dree my weird) of addressing once again the Final Year in Medicine. And having brought you thus to the birth, shall the Faculty not deliver? Let me assume therefore that you are in the Chrysalis stage about to break into the radiant glory of the Butterfly on Convocation or Commencement Day and, therefore, as full fledged physicians, Priests of Nature—on the eve of needing a little instruction in Professional Conduct—Medical Ethics. Ethics, are they? And who are ye?

To answer the latter first—and briefly:—Embryo Physicians—Priests of Nature, who seek out all her secrets on every line and endeavour to employ the knowledge so acquired to the advantage and the good of man in health and in disease. And you must never forget that prophylaxis is more important than therapy, as "the Ounce of

prevention is better than the Pound of cure." And since Medical Men (Physicians, rather) must come into professional contact with all sorts and conditions of men, under all circumstances, and must be prepared to meet them on their own grounds, and varying planes of understanding, they must be possessed of a broad education, universal sympathies and interests, wide experience and wider reading, and so come nearest of all men to Bacon's boast that he had "taken the sum of knowledge for his part."

This is a large order that I place before you, but, "ex necessitate rei," it cannot be exaggerated. To his patient as to the public at large, he must be, if he live up to his calling "Guide, Philosopher and Friend" from the Cradle to the Grave—or as the Old Greek said, "From the Cerement of the Seed to the Cerement of the Grave." The responsibility of no man, not even the Priest, is equal to his. He stands at the two portals of life, and has the responsibility of the safe transition to favour or to fail.

"All the World's a Stage, and all the men and women merely players. They have their exits and their entrances and one man in his time plays many parts," and the Physician is more than Prompter.

"You spake a word too much, my sage,
Of Seers first, and first of Sayers,
For only half the World's a Stage,
And only all the women players."

And to carry the simile a little further—the men are Puppets of the Players.

Bacillus Subtilis*

A certain bacillus, who dines upon hay,
Has quite a remarkable humorous way—
With mirth he will frequently fill us;
It's not of the kind that loud laughter provokes,
The boisterous jest, or the practical hoax,
It's not always easy to follow his jokes—
He is such a subtle bacillus.

The first prize for subtlety—so we are told—
Was given at first to that tempter of old,
The tales of whose cunning still thrill us;
But the serpent, most subtle of beasts of the field,
Had he known what the microscope since has revealed,
Would have hastened at once to this rival to yield—
He is such a subtle bacillus.

He's not pathogenic, pathologists say,
His subtlety doesn't affect him that way,
He's no wish to harm or to kill us;
He did once do harm of a very mild sort—
A conjunctivitis the text-books report—
He must have been pulling their legs just for sport,
He is such a subtle bacillus.

He doesn't do much in the blood-curdling line,
He lets the bacillus cadaveris shine
In deeds which unman us and chill us:
Such methods a cheap popularity buy;
It's not on sensations like that he'll rely;
No, jests such as follow are more what he'll try,
He is such a subtle bacillus.

The candidates in an exam. he'll confuse
By hiding himself in the cultures they use—
They say: "This will certainly pill us,
We've never seen anything like it before;
We'll call it an anthrax without any spore!"
So they do—and are pilled for their pains by the score.
He is such a subtle bacillus.

And then he will waggishly go and invade
A virulent culture which someone has made
Of germs that attack us and kill us,
And when one makes films, and has stained them with Gram,
He'll appear on the slide and say: "Guess who I am!"
And the bacteriologist sometimes† says "Damn!
It's that devilish subtle bacillus."

R.B.P.

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*Reprinted from Round the Fountain and St. Bartholomew's Hospital Journal, April, 1912.

† Oh, surely never!—Ed.

Amputations, Ancient and Modern

A LECTURE TO THE STUDENTS OF McGILL

By W. E. Gallie, Toronto.

FOR those who are interested in the history as well as the practice of our science there is no more interesting pastime than tracing through the ages the changes that have occurred in some particular surgical procedure. Not only does it give us hours of enjoyment but by taking us into the days of the past, as students of the great master surgeons who have given epoch making contributions to our store of knowledge, it stimulates in us an eagerness to attack the problems which remain unsolved today. The subject of my lecture is one well suited to this method of study, for the operation of amputation dates back to earliest antiquity and the changes which have been made at widely separated intervals, intervals which sometimes occupy hundreds of years, stand out on the pages of history with vivid distinctness.

Of the first amputations we have no knowledge, but that the operation was performed successfully long before historic times is certain, for our archeological museums contain specimens of human bones which show that amputation has been performed and that healing of the stump has occurred. The earliest writers refer to it as one of the principal operations of surgery and they recommend it for the same conditions for which it is employed today, namely, severe lacerations of the limb from which recovery is impossible, for gangrene, and for tumours or diseases which destroy the usefulness of the limb and endanger the life of the patient. They point out, however, that the expedient is a desperate one and only to be employed when all other hope of saving the patient's life is gone. That this was wise advice there can be no doubt when one considers the dangers from shock, haemorrhage and sepsis which must have been present in every case. Of descriptions of these operations there are many but more can be learned from the artist's brush than from whole books of words. The plate shows an amputation of the leg in the 16th century

Fig. 1. *Amputation of the leg as performed in the sixteenth century.*

somewhere about the time of Henry VIII. The patient is sitting up, strapped to a chair to prevent struggling. His head is falling backward or to one side as if he has fainted away or is under the influence of some narcotic drug. Opium and alcohol were favorite analgesics. Note the horror-struck countenance of the assistant as he watches the saw pass through the bones and beholds the blood gushing from the severed arteries into the convenient tub. Note also the fillet tied about the limb to guide the surgeon's knife which has been laid aside on the table along with the ligatures which will

be used to tie the bleeding vessels. Most interesting of all, however, is the face of the surgeon who is tackling his job as a good surgeon should, his whole soul wrapped up in the work in hand. Why he insists on wearing his hat is not apparent but if he were asked he might maintain that his own hat is more becoming than the caps we wear today.

How different this scene from that in our modern operating rooms! Think of the agony of the patient who must submit to such an operation without the aid of anaesthesia. How many of these poor sufferers must have died of haemorrhage before the flow of blood could be stanched by searing of the stump with hot irons or tying the vessels with the ligature. And think of the infections which surely developed from the ligature, the knife and the saw. No wonder the surgeon

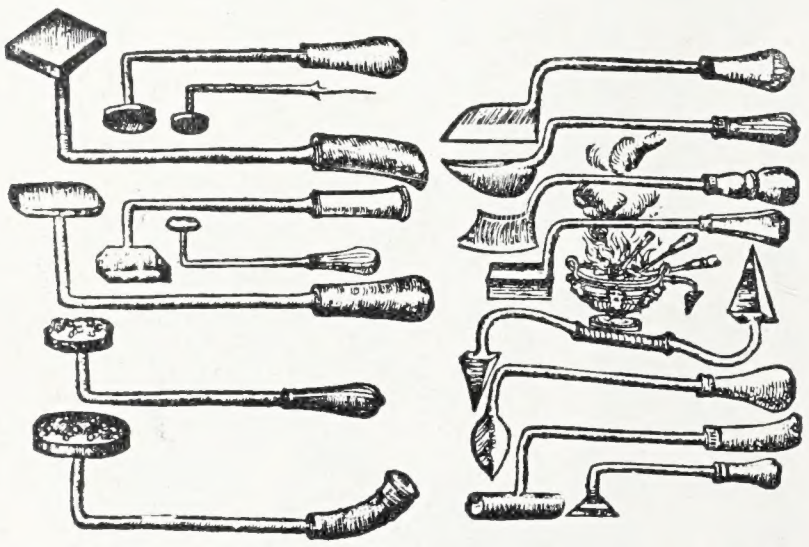

Fig. 2. *Ancient cautery irons and brazier used in the stanching of haemorrhage, before the introduction of the ligature.*

reserved such operation for only the desperate cases. One has only to think of scenes like this to realize the advance that surgery has made in the past five hundred years.

Lest we should scorn our confrères of the past, however, it is well to remember that the great men who have made it possible for us to perform such operations without discomfort to the patient or danger to his life, also belong to the past. And for the ordinary surgeon of former days it must be said that with the knowledge at his command he made the very best of it. Speed in operating was the prime essential and I venture to say he would laugh if he could see us spend an hour over an amputation which he has performed in less than a minute.

The epochs in the history of amputations are marked by certain great advances which have lessened the danger to the patient and the suffering he must bear or have improved the subsequent function of the limb. These are the introduction of the cautery, the ligature, and the tourniquet; the discovery of anaesthesia and of the bacterial cause of sloughing and suppuration in wounds; and the invention of modern artificial limbs.

When the cautery was first employed or who was responsible for its introduction history does not state, but its use is described in the very earliest writings so that there is no doubt of its great antiquity. It probably was suggested by the observation that severe burns, even those sufficient to char a limb completely, were never attended by primary haemorrhage. The method employed differed materially from that in use in our hospitals to-day where an electric current is used to maintain the heat of the iron or wire, but the principle was the same. The illustration shows cautery irons of various shapes and sizes which were in use in the middle of the 16th Century. Some of the end plates were wide and flat for application to oozing surfaces, some are narrow and elongated for convenience in dealing with wounded superficial vessels and others are cone-shaped and pointed for plunging into the deep recesses into which large vessels retract after section in an amputation. Note the angulation of the neck which protects the neighboring skin from injury and the bone or wooden handle which protects the hand of the operator. The heating of the irons in the brazier must have been a dreadful sight for the patient.

The discovery of the value of the cautery in stanching serious haemorrhage must have made an enormous advance for surgery. Without it no amputation could be undertaken without almost a certainty of death from loss of blood, although occasionally amputations for gangrene had been performed by making the section through the gangrenous tissue close to the line of demarkation. The cautery, however, must have saved hundreds of lives which would certainly have been lost without it and greatly widened the field in which surgeons would be willing to undertake this desperate operation.

The disadvantage of the cautery was the

pain it caused the patient. It was bad enough to have to stand the rapid cutting of the flesh and sawing of the bones, but to have added to this the application of the red hot iron must have caused suffering beyond description. It was this that so impressed Ambroise Paré, one of the greatest surgeons of all time, that during the 16th Century campaigns in France he introduced the use of the ligature. The ligature was known to the ancients and was used to stop haemorrhage in wounds inflicted by swords and arrows but apparently had never been employed in amputation. Paré picked up the bleeding vessels with a clamp and tied them with a fine strong thread, leaving the ends long so that they hung out of the wound.

It should be remembered that no attempt was ever made to suture the skin edges over the stump, no matter whether cautery or ligature was used, as experience had shown that the subsequent suppuration would prove disastrous to the patient. The wound was left wide open therefore, in much the same way as in our guillotine amputations during the Great War. The only precaution taken was to draw up the skin tightly before incising it so that when the amputation was complete the skin hung loosely over the ends of the severed muscles and bone and so reduced the time necessary for the ultimate healing.

The pathological change consequent upon the use of the cautery and the application of the ligature was much the same. In the case of the cautery all the tissues to which it was applied were literally cooked and the dead tissue so produced slowly sloughed off as in superficial burns seen in hospitals today. Following the application of the ligature the portion of the vessel distal to the thread underwent necrosis and was finally cast off as a slough. After the lapse of a week or ten days the surgeon daily tugged on the ends of the ligature until finally it came away. The great advantage of the ligature rested first, on the great reduction of the pain and shock, and second, on the comparative unimportance of the sloughing which was produced. Secondary haemorrhage of course was common enough after both methods of treatment, as the infection of the wound might at any time cause the erosion of a vessel, but experience soon showed that after the application of the ligature the danger from this source was much reduced.

Fig. 3. *Ambroise Paré, at the age of forty-five. He was the first to use the ligature in amputations.*

As is the case with all great reformers, Paré was subjected to much virulent abuse, and many pamphlets were published by his conservative confrères attacking the method he described; but the preeminence of the man in his profession and his ability with his pen as well as his scalpel swept all opposition aside and since his time the cautery has not been used to stanch haemorrhage in recent wounds.

At the age of forty-five Ambroise Paré was the leading surgeon of his time. He rose rapidly from post to post until he was surgeon-in-chief of the French army and principal surgeon to the king. His published books on the treatment of wounds and on dislocations rapidly became the standard works of all western European countries. He is said to have devised the operation of podalic

version. But through all the ages he will be remembered as the man who did so much to reduce the horrors of war by the introduction of the ligature. His face is that of a strong yet gentle man from whose lips one might expect the expression he so frequently used in reciting his histories, "Je le pansait, Dieu le guerit," "I dressed him and God healed him."

Surprising as it may seem, history contains no mention of the tourniquet till the latter part of the 17th Century. How surgeons got along without it or why nobody thought to employ it is difficult to understand, but the fact remains that it was not used until comparatively modern times. When first introduced it consisted of a strong, narrow band which was tightened circularly about the limb by twisting it with a short stick. In 1718, however, a French surgeon named Petit introduced an instrument which was a vast improvement on the older constricting band and which, until the recent invention of the rubber tourniquet, was almost universally employed. It consisted of a narrow wooden and later metal plate which was pressed-down upon the main artery of the thigh or arm by means of a coarsely threaded screw. The advantages of this instrument are obvious as it did away with the pain and laceration produced by the constricting band. It was so simple of operation that it could be left loosely applied on the limb of the patient in whom secondary haemorrhage was feared and could in case of necessity be screwed down by the patient himself. I can remember well seeing it used in the old General Hospital in Toronto when I was a house-surgeon there. With the introduction of general anaesthesia, however, and the invention of india rubber the need of Petit's tourniquet passed away and its place has been taken by the simple rubber band or by the pneumatic tube which can be inflated until the pressure is sufficient to stop the circulation of blood in the arteries.

The introduction of the tourniquet must have marked a great advance in the surgery of amputations. Occasionally it is necessary to perform an amputation without a tourniquet owing to hardening of the arterial walls, but even in our modern operating rooms where complete anaesthesia makes it possible for the surgeon to move slowly and to pick up the vessels as he meets them, the haemorrhage is severe. Before anaesthesia, however, where speed in getting the limb cut off was the chief object of the operator, the haemorrhage must have been tremendous before the vessels could be sealed off with the hot iron or tied with the ligature. With the tourniquet the loss of blood is negligible.

While the cautery, the ligature and the tourniquet did much to make the successful amputation of gangrenous or grossly diseased limbs possible, it remained for the 19th Century to remove from this frightful operation most of its terrors and to widen enormously the field in which it could be wisely employed. On November 7th, 1846, Wm. T. G. Morton, a dentist in Boston, placed a patient under the influence of his new anaesthetic, sulphuric ether, while Warren, one of the surgeons of the Massachusetts General Hospital, in Boston, performed an amputation of the leg. The patient made no movement or complaint during the operation and when he awoke from his sleep had no recollection whatever of what had taken place. This demonstration marked the greatest advance that had yet been made in the surgery of amputations. To the patient the relief from suffering was a boon beyond description. For the surgeon it removed the nerve-racking horror of the situation and made it possible for him to dispense with the reckless speed which so frequently destroyed the perfection of his work.

Despite these advances, however, amputation still remained an operation to be dreaded by the patient and surgeon alike. With almost perfect regularity the wound went through the stage of heat, redness, swelling and pain and at the end of four or five days was a mass of pus and corruption. Erysipelas, gas gangrene, malignant oedema and lockjaw were common precursors of a miserable and pitiable death. Even in the ordinary suppurative cases the danger of fatal secondary haemorrhage was always present and if the patient had the luck to avoid these disastrous complications his convalescence was prolonged and tedious.

But with the beginning of the second half of the 19th Century a glorious change was at hand. About the year of 1861 Joseph Lister of Glasgow began to teach that suppuration in wounds was due to contamina-

tion with the minute living organisms which had recently been shown by Pasteur to be the cause of decomposition. To a man of Lister's abilities it was a matter of a single step to pass from this great principle to the discovery of a method of preventing contamination. From the experiments performed in the laboratory and the wards of the old Glasgow infirmary in 1865 has developed the whole system of antiseptic and aseptic technique which is the most important feature of our surgical training today. With the dawning of the era of the sterilization of dressings, instruments and skin the fetors of the surgical ward ceased to offend the sweetness of the atmosphere and the infection of wounds gave place to healing by primary union.

The influence of the discoveries of Lord Lister on the surgery of amputation was enormous. The operation can be undertaken now without fear of septic infection and without the dread of secondary haemorrhage. The ligatures which formerly were left long in order that they might be pulled off when the slough had separated can now be cut short and buried in the wound and the wound itself can be confidently closed without fear of disastrous results. The convalescence of the patient has been reduced from months to days and when the dressings are removed the stump is smoothly covered with skin and is ready for preparation for the fitting of an artificial limb.

Previous to the developmeut of antiseptic and aseptic surgery little progress had been made in the construction of artificial limbs. The chief reason for this was, in all probability, that the demand for them was small. From the short review I have given of the difficulties and complications which surrounded the operations it will be realized that many more calls would be made on the undertaker than on the maker of artificial limbs. Further, the scarred, puckered and painful stumps that were left were altogether unsuitable for fitting into any kind of a socket. Our own experience in the late war has shown that this statement is perfectly true as approximately half of the soldiers who had had amputations done in the dressing or casualty clearing stations had to have reamputations performed before an artificial limb could be applied. In pre-antiseptic days

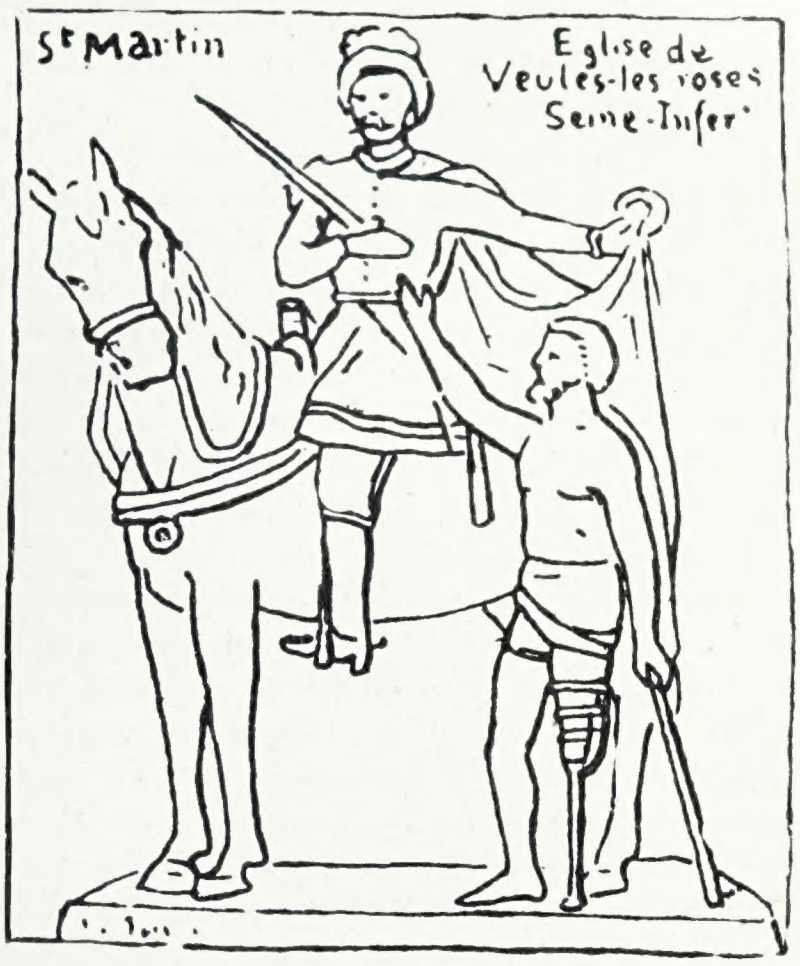

Fig. 4. *Drawing of sculptured group done in the 13th century. It shows a man who has had an amputation through the thigh, and the peg leg provided as a substitute.*

no one would take the risk of re-amputation for the purpose of improving the stump. A third reason for the slow progress of the industry was a purely economic one. Loss of limb is an accident which occurs, in the vast majority of instances, among the poor, and a good artificial limb is an expensive instrument. I can recall quite distinctly several laboring men in the town where I was a boy, who were forced to hobble about on peg legs for the rest of their days simply because they had no means of getting better ones. Nowadays, however, at least in civilized countries, the pension commissions, the Workmen's Compensation Boards, and the charitable societies have made it possible for every man, woman and child who has lost a limb to be provided with a suitable substitute. Hence the business thrives.

The influence of the rise of the modern artificial limb on the surgery of amputations has been very great. In former days the chief aims of the surgeon were to save as much of the limb as he possibly could and to so arrange the stump that the patient could ultimately carry his weight on the end of it. The drawing is taken from a sculptured group done in the 12th or 13th Century and

shows a man standing on the end of the stump of his thigh amputation in just such a peg leg as was common twenty years ago. The only exception to the rule that the limb should be left as long as possible was in the case of amputations between the ankle and the knee. Here the section was always made a hand's breadth below the joint, in order that the patient might kneel in his stump socket and yet not have the end of the flexed stump of the leg projecting backward beyond the thigh. This was called "amputation at the seat of election."

Modern artificial limbs have completely changed the viewpoint of the surgeon. His aim now is, or should be, to perform his operation in such a way that a satisfactory limb may be fitted and worn. Over and over again I have known patients with what we now know to be defective stumps try limb after limb, only to be forced in the end to go through another amputation. No surgeon is competent to amputate a limb who has not a clear idea of the substitute he proposes for it. The time to consult with the limb maker is before the operation is performed, not after the deed is done.

The modern student may not know it but he is under the deepest obligation to the makers of artificial limbs. While making the notes for this lecture I looked once more into the pages of that standard text book on Medieval Surgery, Rose and Carless, and I find there described eighteen different amputations of the lower extremity. Of these, the artificial limb maker will tell you that only four are of any value. The operations of Lisfranc, Hey, Chopart, Perrin, Pirogoff, Faraboeuf and Steven Smith, while intensely interesting to the student of history, have no place in the surgery of modern amputations. Do not waste valuable time before your examinations in reading about them as they will soon disappear from the text books. The operations which lend themselves to the prosthetic appliances of today are Syme's amputation just above the ankle, amputation through the middle of the calf, the Gritti-Stokes amputation at the junction of the condyles with the shaft of the femur and an amputation through any point in the thigh which leaves a stump long enough to be grasped by the socket of an artificial limb. Amputations through any portion of the tarsus or through the ankle joint, at the seat of election, or through the knee or the hip leave stumps to which no really satisfactory limb can be fitted.

Before dealing with these four special amputations a word should be said of the principles which should act as a guide to the operator. The old idea that a stump should be made as long as possible must be modified. It may be taken for granted that unless the end of a stump is doing something, such as carrying weight, or is situated close to a functioning joint, it will get blue and cold and sometimes oedematous as it lies motionless in the socket of the artificial limb. Where it is not the intention, therefore, that the patient shall carry his weight on the end of his stump, the limb should be cut off as short as satisfactory activation of the artificial limb beyond the nearest functioning joint will allow. Thus a long stump in a below-knee amputation is unsatisfactory for the reasons described above and is not nearly so good as a stump in which the tibia is divided six inches below the knee. The same objection to a long thigh amputation does not exist, however, as here the circulation is better maintained.

Wherever it can be made possible for the patient to carry his weight painlessly on the end of his stump this result should be strived for. It has been found that patients who are able to do this walk more naturally and can stand and walk continuously for longer hours than patients who transmit their weight to the artificial limb along the sides of the stump. Thus the Syme and Gritti-Stokes stumps are better than those left by amputation through the calf or the middle of the thigh.

A detail of the operation which must never be forgotten is to strip every nerve that can be found, for two or three inches, and to cut them off cleanly so that their severed ends are far removed from the scar tissue which will form over the end of the divided muscles. If this detail is neglected endless trouble will arise from pain in the neuromata which form on the ends of the nerves.

After the muscles have been divided with clean sweeps of the knife, so as to avoid all unnecessary damage to tissue, they should be drawn upward with a retractor and the bone

divided at such a level that the sectioned ends of the muscles, when they have undergone retraction, lie in the same plane as the end of the divided bone. Before sawing the bone the periosteum should be reflected from a lower level so that when the sawing has been completed a flap of periosteum will drop over the anterior edge of the bone and so prevent the skin from adhering to it. loosely. This is important, particularly in stumps in which weight bearing will be along the sides, as with each step the skin will be drawn upward. If the flaps are too tight cracking and ulceration of the scar will result. The flaps should not be redundant, however, as puckering may result and the sweating which occurs in the pockets will give just as much trouble as does shortness of flaps.

Fig. 5. *Stump of Syme's amputation and the artificial limb devised for it.*

Nothing is more distressing to the patient than the tugging of the skin on an adherent scar. In the case of the tibia the anterior edge of the sectioned bone should be bevelled off with a chisel to prevent ulceration of the skin where the end of the stump strikes the wooden shin of the artificial leg. The fibula should be cut off an inch shorter than the tibia as this narrow bone is apt to act as a spear.

The skin-flaps should be long enough to close over the ends of the bones and muscles Where it is intended that weight shall be borne on the end of the stump, no scar should cross the weight-bearing area. Where lateral bearing is intended the scar is better placed on the end than elsewhere.

In regard to the operation of Syme there is some difference of opinion.* It was devised about the middle of the last century

*The photographs of amputation stumps and artificial limbs have been taken from the paper of Dr. A. B. LeMesurier, Journal of Bone and Joint Surgery, April, 1926. For further details in regard to modern amputations the reader is referred to this excellent paper.

by the professor of surgery at Edinburgh for the purpose of getting rid of tuberculous disease in the ankle-joint. The expanded lower ends of the tibia and fibula are left in the stump and these are covered with the thick skin of the inferior and posterior aspect of the heel. The limb makers are not fond of the amputation because it is impossible to build a limb to fit the bulbous end of the stump which will exactly simulate the normal. The appearance of the limb is not so bad in the case of a man, for the thick ankle is hidden by his trouser leg, but it is nearly impossible to persuade a woman to put up with it. The tremendous advantage of this type of stump over all others, however, is that the patient can jump out of bed and walk about the room without bothering with his artificial foot. Further, as this is an end-bearing stump, situated close to the ground, the patient has greater security in walking and has a much better gait than with any other kind of amputation. A short time ago I was well beaten at squash-rackets by a gentleman who had had a Syme's operation.

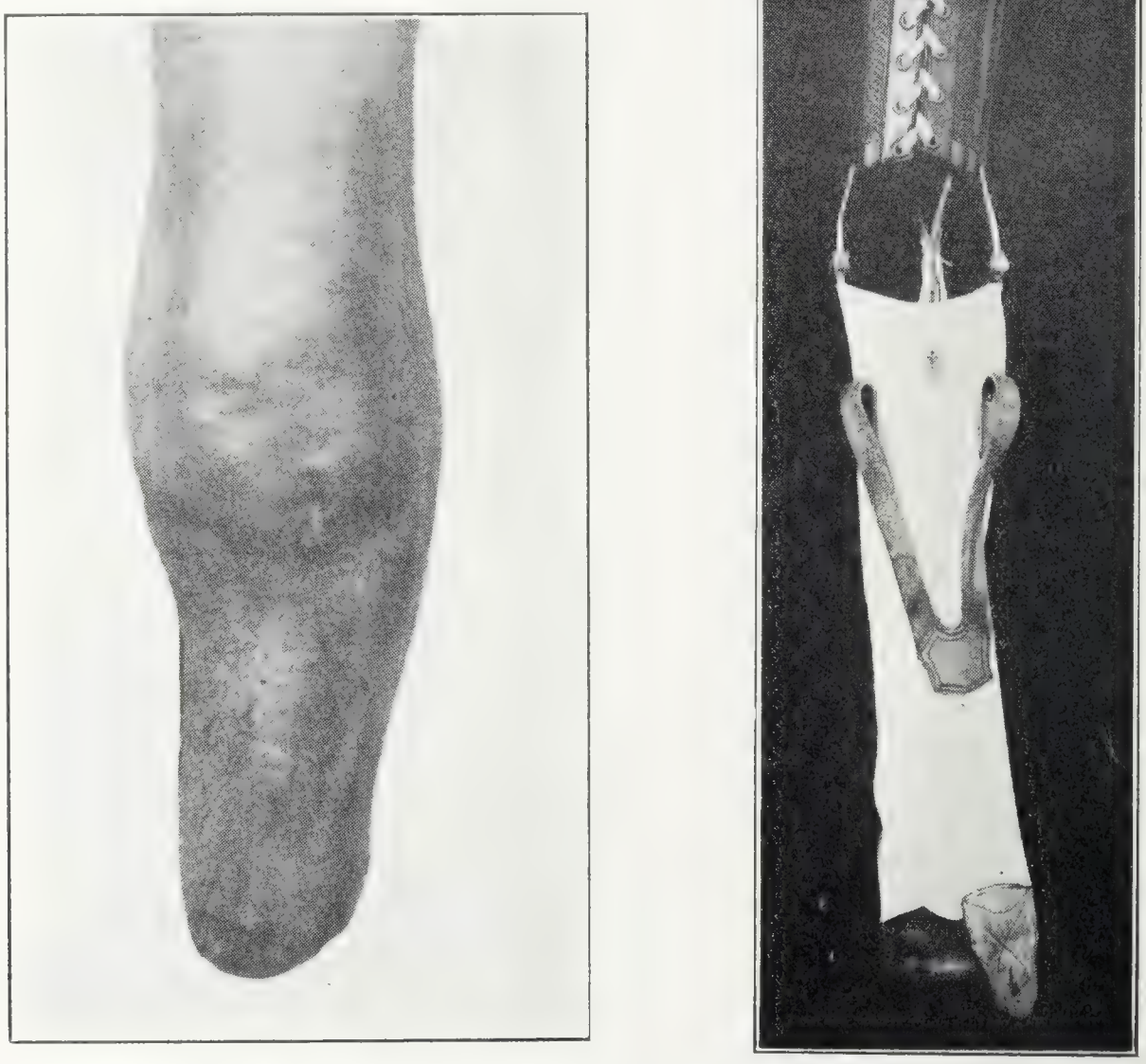

Fig. 6. *Stump of an amputation through the middle of the calf and the artificial limb devised for it.*

To result satisfactorily, however, a Syme's amputation must be very carefully performed. The nerves must be cut far back to make sure of preventing painful nerve buds; great care must be taken to avoid wounding the posterior tibial artery above the branch which supplies the flap; and the flap of skin must fit accurately over the bones without tightness or redundancy. A loose flap will result in a stump in which the end will wobble with every step and the patient will suffer constant discomfort. A successful Syme's amputation, on the other hand, when a good artificial foot has been applied, leaves only the smallest amount of disability and from the standpoint of continuous weight-bearing is the best amputation that has yet been devised.

Amputation through the calf is the operation which the limb-maker prefers above all others. It leaves him a stump which he can fit with a limb which will often defy

detection. The artificial limb is wonderfully satisfactory and a veritable triumph for the limb-maker's art. The first illustration in fig. 6 shows an excellent stump which has stood the test of years in a stump-socket, and the second shows the limb designed for it. The shin piece or socket is made of willow, accurately modelled to the shape of a leg. This socket is carefully hollowed out, from measurements and comparison with a plaster cast, until it is so shaped that the stump will fit snugly into it and rest its weight on the expanded upper end of the tibia and along its lateral surfaces. To the lower end of this socket is attached a well modelled wooden foot provided with a joint at the ankle and another just behind the toes, and from the upper end

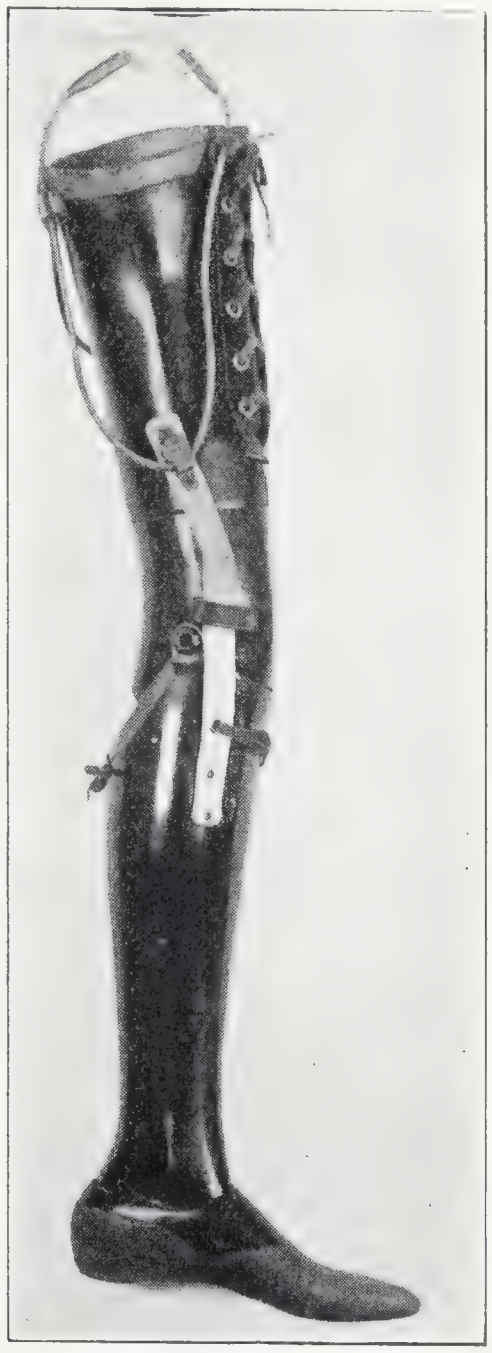

Fig. 7. *Gritti Stokes amputation. The patient takes the whole of his weight on the end of the stump. The bucket of the artificial limb is made of leather, which is laced down the front.*

two steel bars, jointed at the knee for motion, pass upward to be attached to a cylindrical leather lacing which incorporates the thigh. So perfectly does this applicance take the place of the natural limb that the wearer can frequently take his place in society without suspicion that he has lost a limb. A few weeks ago I saw a play called, "These Charming People" and I was astonished to learn afterwards that one of the principal actors had had this amputation. It is said that one of our first contingent got past the medical examiners and ultimately reached France before it was discovered that one of his legs was wood. With all its perfection, however, this amputation has its defects. With all the weight supported on the skin over the condyles of the tibia and the lateral aspects of the stump it is rare indeed to see a patient who can stand through an eight hour day. When it comes to endurance the Syme's stump has a decided advantage, and even the end-bearing Gritti-Stokes stump, where the limb is sectioned above the knee, is better adapted for long hours of standing at a bench or a machine. But for the doctor, the lawyer, the business man

Fig. 8. *Artificial limb for an amputation through the thigh. The bucket is made of willow, which is accurately fitted to the sides of the stump and the tuberosity of the ischium where the weight is carried.*

and for most women the amputation through the middle of the calf is so satisfactory that little is left to be desired.

Loss of a limb above the knee was, until the development of modern artificial limbs, a disaster of the first magnitude. It destroyed all possibility of earning a living, for the patient was usually condemned to depend for locomotion on crutches or a wheel-chair. But the artificial limb of today has completely changed this dismal outlook. The patient can now look forward to a fairly comfortable existence and, if he has had the luck to have the Gritti-Stokes operation performed, to a prospect of competing on a fairly even basis in the ordinary labor market.

The Gritti-Stokes amputation is made through the femur at the junction of the condyles with the shaft and on the end of the stump of the femur so produced is laid the freshened surface of the patella. When healing takes place the patient finds himself with a stump, the end of which is smooth and rounded and which, owing to the presence of the patella on the end of the femur, will allow him to stand with the whole of his weight on the end of it. Our experience with soldiers and later with civilian patients, particularily with those suffering from diabetic gangrene of the foot, has taught us that this is far the most satisfactory amputation of the thigh.

While the below-knee leg is an excellent instrument, the above-knee leg is really a marvellous invention. Not only does it provide the patient with a comfortable and efficient support but it affords him the advantage of a flexible foot and a knee in which the motion is under his immediate control. With practice these patients can walk with only a moderate limp and if the stump is an end-bearing one they can stand all day at their work. The feature of the limb is the scheme by which the knee is controlled. The joint is so constructed that it comes to a dead stop when it has been extended slightly beyond the straight line. This slight degree of hyperextension provides against sudden collapse when weight is borne on the extended limb. By arranging the joint in the ankle so that the foot is in slight equinus and cannot be dorsiflexed quite to the right angle, a lever is provided by the foot and the shin which shoots the knee back into hyperextension as soon as the foot strikes the ground. Additional stability is lent to the knee also by a spring in the interior of the joint and a lever to which is attached a strap which passes up over the patient's shoulders, and which when the back is straightened becomes taut and acts very much like the quadriceps muscle. These devices make it possible for the patient to flex and extend the knee at will and are the secret of the success of the limb.

A word must be said about the preparation of the stumps of all amputations for fitting with artificial limbs. During the months which follow the healing of the stump a slow but steady shrinkage takes place owing to the atrophy of the functionless muscles. To provide a patient, therefore, with an artificial limb soon after his amputation will

prove very expensive as the shrinkage of the stump will soon destroy the fit of the limb. The process of shrinking can be hastened by keeping the stump bandaged with some elastic material. A scheme which has worked out well in the military and compensation board cases is to provide these patients about two months after their operation with some cheap form of pegleg which will encourage the process of shrinking as well as allow the patient to get about.

In this lecture we have traced through the ages the development of a single surgical procedure and have touched on the lives of the great men who have done so much to mitigate one type of human suffering. Surgery is an art which is constantly changing but one in which the true advances come only from the touch of those whose motto is that of Ambroise Paré, "Labor improbus omnia vincit." To the student of today, however, it may be said that as a science it is only in its infancy, and that the opportunity is as great as ever to emulate the work of the masters who have stamped their fame upon the pages of time.

Bones and Their Significance.

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USUALLY to a student in the medical course, human anatomy is the first subject of study which is directly associated by him with his future professional work, and in most cases the first work in anatomy with which he comes into contact is osteology. The study of the bones of the human skeleton appeals to him only as a dry uninteresting array of facts to be somehow or other retained in his memory. The first application of these facts is realized during dissection and slowly and steadily throughout the clinical work it is increasingly impressed upon the student what an important part of the body the bones and their joints comprise. Finally there stands in the young graduate's mind a great array of facts regarding the bones in relation to fractures, dislocations, bone diseases, necrosis and other conditions.

In spite of this accumulated knowledge first impressions in many cases tend to remain and a bone is still regarded as something hard, inanimate, altogether set apart from the remainder of the body tissues, and forming merely a passive support for them. One of the objects of this paper is to combat this impression produced by the constant examination of the dried, specially prepared skeleton and to look upon bone in the living body just as any other tissue is regarded, forming an organ very much alive and with the properties and requirements of living tissues. Here it should be noted that bone cannot be produced in any way except in the living bodies of the higher animals, and it is vital, full of life, not just a passive inert piece of scaffold or framework on which the living tissues are supported. The evidence of this life and its accompanying activity are numerous and are shown in many different ways.

In the first place it is to be noted that bone is an actively growing tissue and shows just as remarkable changes from infant to adult as do other tissues. It changes its size and its shape, assimilates to itself new material, and for its activities it is supplied with blood vessels, lymphatics and nerves in a similar way to all other living tissues. Bone can die, and when it dies the portion from which life has departed is known as an area of necrosis and it is sloughed out of the tissues and got rid of by the body just like any other foreign body.

Without the skeleton the body would be a shapeless, flabby mass. Through the rigidity of the bones definite form and proportion are maintained, and on this framework are fastened the muscles. Muscles, bones and joints form a very interesting and intricate system of levers by which one part of the body is moved upon another, or even the whole body is moved from place to place. The working of these levers is in accord

with the known laws of physics applied to such structures.

As most bones require to expose a large surface without the necessity for the interior to be solid, we find stored in the interstices of the cancellous bones the red marrow, which might be called the blood factory of the body, continually manufacturing new red blood cells in particular. Nature shows a wonderful economy in using this space, so wonderfully protected from stresses and strains and where a sluggish, slow-moving stream can have the corpuscles added to it as boats might be shoved out on the protected bays of a rapid river in order to be caught in the stream.

Bone, while quite hard, is not as brittle as one tends to think, but possesses elasticity which allows it to bend and yield slightly to strains and then resume its original shape again. It shows the strength of a piece of white oak of the same size, or about one quarter the strength of medium tough steel to the forces of tension, compression and shearing.

Chemical analysis shows that bones are one third organic material, known as ossein, which yields gelatin on boiling. This it is which provides the elasticity. The rigidity is produced by the inorganic material, two-thirds of the mass of the bone, composed of fifteen parts by weight of calcium carbonate to eighty-five parts of calcium phosphate, with traces of fluorides and magnesium salts.

Microscopic analysis of bone reveals the living elements, layers of cells isolated and buried in the matrix of ossein and calcium salts with which it has surrounded itself, but retaining communication with blood vessels or with other cells through fine canaliculi by which it draws its nutrition. The matrix is presumably inert but is not unchangeable after its formation, for it alters with the state of health and activity of the bone.

To provide for proper growth in a young bone several factors have been shown to have importance. In the first place good vitality in the osteoblasts and bone cells is a prime necessity, and anything lowering their activity results in a lessened rate of growth. Plenty of food and building material, good, rich blood carrying plenty of calcium and phosphates, is required and if this supply is limited defective development results. If defects in the supply of material is complicated by lack of vitamines in a young child then true rickets will result, and in older persons osteomalacia occurs. The vitamines and also tonics stimulating cellular activity, and administration of calcium salts and phosphates stimulate bone formation. This process is also favored by ultra-violet light, and exposure to sunlight.

The hormones of the ductless glands have a marked effect on the skeleton, and the size of the bones and the number of years in which growth is possible before epiphyses close is controlled by the pituitary, gonads, thymus, thyreoid and adrenals. Dwarfism may be a hypopituitary effect and giantism the result of hyperpituitism, while acromegaly shows the effect of a disordered action of the pituitary gland. The tall stature of eunuchs and the late union of epiphyses is an example of the effect of the loss of the hormone from the sex gland.

Even adult bone still requires a certain upkeep. All through life its bone cells are alive and working, maintaining the integrity of the matrix which is continually being kept in repair by what is sometimes called a creeping replacement. The calcium content is not fixed, but is labile, and is quickly changed. A pregnant woman often shows rarefaction of the cancellous tissue of her bones due to the heavy demand for calcium by the foetus with its rapid development. A limb put in a sling shows distinct rarefaction of its bones when kept at rest for a few weeks.

The amount of development in a bone, the height of its muscle prominences, the size of parts bearing strain or weight are in proportion to the amount of strain, provided this is within physiological limits. Growing bones respond to strains by increased growth, therefore good skeletal development depends upon muscular exercise, and the proper shape and proportion depends upon the individual maintaining proper posture. Improper posture puts strain on the wrong places, a physiological growth response ensues and the skeleton is adapted to the posture and deformity results.

The skeleton is most wonderfully adapted

to the work it has to perform. Joint surfaces are always expanded to distribute the strain over a fairly large area and within the bone cancellous plates are ranged closely approximated in the main lines of force, and are tied and prevented from buckling under strain by other plates across these lines. Compact bone forms only a thin shell covering in the cancellous bone everywhere except in the shafts of the long bones. Here the forces are well carried in the thick, compact, pillar-like shaft, but the ends are always expanded and cancellous as there is more strain to be taken up here in all directions.

Bones are plastic in life and will change their shape in response to strains long continued, even in the adult. This is seen in the changes found in flat foot. As the arch of the foot falls those parts of the joint surfaces not now in use disappear, while the new areas of contact developed adjacent to the rest of the joint become covered by an extension of articular cartilage, and so the joint appears to actually migrate over the bone. The actual shape of the bone as well as its relations may gradually change also.

Bones further exhibit their vital functions in the repair of injuries. Areas lost by inflammation and injury are filled in with new bone. Fractures are cemented by immediate production of callus which is then converted into new bone and fully completes the repair so that the bone is again a unit, as strong as ever, sometimes stronger than before. Large masses, such as the greater part of the shaft of a tibia may be replaced after the death and removal of the original part.

Bones are subject to inflammation and to infections and may be destroyed by diseases, such as tuberculosis or syphilis, and may show death of large parts, a condition known as necrosis. These are all evidences that bone is a living, active tissue like the other tissues of the body and is to be treated as such.

There is a medico-legal aspect of importance in connection with the skeleton. As the bones are the hardest structures in the body they are the last parts to decay and disappear. They last much longer than any of the other parts and so may form the only evidence of the former presence of a human body in a certain place.

Where attempts have been made to destroy a body by fire the bones may still be found even when the other tissues are consumed, being preserved from total destruction by their content of incombustible inorganic material formed by the calcium salts. Many of the bones of the human body have distinct, easily recognizable characters marking them out as human, so that it is possible to make definite statements at to the identity of the remains as being part of a human body.

It is also due to the evidence of the bones that we have any knowledge as to the stature, type of body and shape of head of prehistoric man. Many fossils of lower animals and plants have left the impression of the softer parts of their bodies as well as their hard parts and skeletons preserved for us in the rocks. We thus have a very good idea of their external form and appearance. But of the earliest men on the earth we have only the evidence provided by bones and teeth.

As we approach modern man we find many evidences of culture along with the remains, such things as arrow heads, knives, pottery and other implements. Of the cave men we have drawings on the cave walls and also carvings on ivory as still living records of the men and animals of that period. From the dawn of history we have an ever-increasing series of records of various kinds to show us man's appearance in each age, but of earliest man there remains only parts of his skeleton.

Now it is possible, given various parts of the skeleton, to reconstruct a whole individual and this reconstruction is particularly exact in rebuilding the whole skull from a part, and the head from the whole skull. From the remains of prehistoric man reconstructions have been made to give us some idea of these most interesting remote races. Their appearance must still be partly a matter of conjecture, but if their bones had not been preserved for many thousand years as a heritage to us from the past, we would not have even the actual meagre facts we now possess. From these facts we are able to gather an approximately correct idea of the first men who inhabited the earth.

The Distribution of Blood in the Human Body.

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ESTIMATES of the total blood-volume in man have not been altogether acceptable until lately because the two chief methods, the carbon monoxide method of Haldane and Smith (1) and the dye method of Keith, Rowntree and Geraghty (2) have ordinarily given decided discordant results. However, Lindhard pointed out in 1926 (3) the source of error in the dye method, namely, faulty distribution of the dye to the superficial vessels used for taking blood samples, and showed how by causing the subject to exercise his muscles during the period of distribution this error is avoided. When this precaution is taken the results of the two methods are concordant, indicating the average total blood volume to be in round numbers 5 per cent. of the body weight. In other words, a man weighing 70 kilograms (154 lbs.) may be supposed to have about 3.5 liters of blood in his body.

The interesting question as to how this blood is normally distributed appears not to have been carefully considered. All the text books with which I am acquainted that mention the problem at all are content to cite some old figures attributed to Ranke (4) and obtained from rabbits, which state one-fourth of the blood to be in region "a," i.e. the heart, lungs, and large blood vessels, one-fourth in region b, the liver, one-fourth in region c, the skeletal muscles, and the remaining fourth in region d including all the abdominal organs except the liver, the pelvic organs, the glands of neck and head, the central nervous system, the skin, the skeleton and the adipose tissues. As a matter of fact the actual observations of Ranke showed 23 per cent. of the blood to be in region a, 29 per cent. in region b, 29 per cent. in region c, and 19 per cent in region d. The shading of these data to make the proportions equal is found in Vierordt (8).

Assuming Ranke's data modified to be properly applicable to man each of the above four main regions would be supposed to contain roughly 875 ml. of blood (25 per cent. of 3.5 liters). But there is evidence indicating a decidedly different distribution of the blood in the human body. This evidence I wish to consider briefly in this paper.

Let us look first at region a, heart, lungs and large blood vessels. We have positive evidence furnished by Y. Henderson and Haggard (5) among others that in many normal individuals at each beat of the heart each ventricle discharges on the average slightly over 100 ml. of blood. At the instant when the organ contains most blood, i.e. at the beginning of the atrial systole, it must contain more than 200 ml., and since it is known that the heart does not always empty itself completely at systole and especially since an allowance must be made for the capacity of the coronary vessels, an estimate of 220 ml. can hardly be too high.

Estimates of the blood content of the lungs vary widely according to how they are arrived at. Burton-Opitz (6) states that various observers have estimated the pulmonary circulation time at 12-15 seconds. Since the right heart often discharges more than 100 ml. at each beat and the rate of beat is faster than one a second this implies a pulmonary blood-content of more than 1,200 ml. A similar quantity is indicated by observations on the capillary area of the lungs (Vierordt). From the capillary area the capillary volume can be computed, and when to such a computation an allowance for the capacity of pulmonary artery and pulmonary vein is made we obtain again a figure in excess of 100 ml. On the other hand, direct observations on rabbits and dogs cited by Wiggers (7) and others indicate the pulmonary blood content in these forms to be less than 10 per cent. of the total blood volume. This corresponds in man to a pulmonary blood volume of not more than 350 ml. The larger figures given above are based on data in which estimates are necessarily relied on to a considerable extent. They are, therefore, to be discounted

when in conflict with direct experimental results, and while it is not necessarily to be assumed that the human lung contains precisely the same relative amount of blood as the canine, it is quite unlikely that one should have three times the blood capacity of the other. It appears more reasonable to me to postulate for the human pulmonary tract an average blood content of about 500 ml., thus making some concession to the data indicative of larger blood volume without departing too far from the figures suggested by direct experimentation on lower animals.

In an interesting compilation of anatomical and physiological data by Vierordt (8) a series of measurements of lengths, diameters, and thicknesses of walls of the main arteries is given. From these I have calculated the combined post-mortem capacity of aorta, coeliac axis, common carotids, subclavians, axillaries, external iliacs, and popliteals. The figure, in round numbers, is 170 ml. It is safe to add 10 ml. for arteries not included in the above list, giving a total of not less than 180 ml. for the post-mortem capacity of the main arterial tree. When we bear in mind that in the living body the arteries are distended with blood to a pressure which at its minimum (diastolic) averages 80mm. Hg. or more it is obvious that considerably more than this quantity of blood must actually be present. An unpublished calculation based on the volume input of blood at systole and the pulse pressure indicates that not less than 100 ml. blood above the post-mortem capacity must be present at the end of diastole, or at least 280 ml. in all.

It is certain that the veins have considerably greater capacity than the arteries. Whenever an important artery and vein run side by side the latter is always larger than the former. Furthermore all tests of blood velocity, which is inversely proportional to total cross section of the vascular bed, show that at any given distance from the heart the venous flow is markedly slower than the arterial. Keith estimates that the "venous cistern," in other words the main venous tree, has a capacity of about 400 to 500 ml. If we adopt the minimum figure and assume the venous cistern to contain not more than 400 ml. of blood, we obtain for the blood-content of region "a" the following items, heart 220 ml., lungs 500 ml., arteries 280 ml., veins 400 ml. These total to 1400 ml. or 40 percent. of the entire blood volume, instead of not more than 25 per cent. as estimated by Ranke for the rabbit.

By making the estimates for the various items under a as conservative as seems permissible we then have left for all the other regions of the body an assumed 60 per cent. of the blood volume, or 2100 ml. What opinion can we form as to the distribution of this amount?

According to Ranke's data regions b, c, and d are approximately equal in blood content in the rabbit. If the same equality held for man we would therefore assign to each of these regions about 700 ml. of blood. There is no reason to question the reliability of Ranke's data, as they are the result of direct determinations. Furthermore they have been confirmed in the main by W. Krause (10).

The reason for questioning the applicability of these figures to man is that the relative proportions of bodily substance are decidedly different in man and rabbit. We are justified in assuming that the blood content of any tissue bears some relation to its nutritive requirements in the first place and to its mass in the second. In the rabbit region b, the liver, is stated (Krause) to contain about 25 per cent. of its weight of blood. This ratio is presumably adjusted to the needs of the organ, and may be assumed to hold in general for the human liver. In man the liver weighs about 1899 gms.*; consequently its blood content may be estimated at about 450 ml. (since the estimates are in round numbers no allowance is made for the fact that 1 ml. of blood weighs slightly more than 1 gram). The smaller relative blood content in man as compared with the rabbit is to be accounted for by the fact that the rabbit's liver makes up fully 6 per cent. of the weight of the animal while the human liver is only about 2.5 per cent. of the weight of the body.

The rabbit's muscles contain approximately 2.7 per cent. their weight of blood. The human musculature constitutes about 45 per

*The data on human organ and tissue weights are all taken from Vierordt (8).

cent. of the body weight, or for a 70 Kgm. man about 31.5 Kilos. 2.7 per cent. of this gives for the blood-content of region c about 850 ml. By subtracting the sum of these two estimates from 2100 ml. we obtain 800 ml. for region d. What reasons have we for thinking this figure even approximately accurate?

Region "d" includes the abdominal viscera, exclusive of the liver, the pelvic viscera, the glands of head and neck, the central nervous system, the skin, the skeleton and the adipose tissues. The included viscera and glands have a total mass of about 2500 grams and according to Krause's data on rabbits appear to contain about 5 per cent. their weight of blood, or about 125 ml. The human central nervous system weighs about 1450 gms. on the average, and is said to contain also about 5 per cent. its weight of blood in the rabbit. Again applying this ratio to the human body we obtain an estimate of 75 ml. for the central nervous system. The skin of the rabbit (the hair included) appears to contain about 1 per cent. its weight of blood. In view of the relative unimportance of the fur clad skin for temperature regulation as compared with the naked human skin it seems reasonable to assign double the above percentage to the latter. The skin is estimated to weight about 4800 gms. in a man of average size. Two per cent. of this gives us approximately 100 ml. for the blood content of the skin.

The rabbit's skeleton is stated by Krause to contain about 8 per cent. of the blood of the animal; or for specimens of the size studied by him, weighing on an average 1300 gm., and containing about 70 ml. of blood, a content of about 5.6 ml. The skeleton itself in a rabbit of that size weighs about 160 gms. Consequently the skeletal blood amounts to about 3.5 per cent. the weight of the skeleton itself. This might seem an unbelievably high percentage were it not for the fact that within the skeleton is included the blood-forming red marrow, probably one of the most vascular tissues of the body. The human skeleton weighs about 11,000 gms. on the average. If we assume it to contain the same proportional quantity of blood as in the rabbit we have 385 ml. as the amount of skeletal blood in man.

Summing the above items of region d, we obtain a total of 685 ml., with the adipose tissue, weighing something like 13,000 gms. in an average 70 kilogram man, unprovided for. If these tissues contain as much as 1 per cent. of their weight of blood, which is fairly likely, the content would be about 130 ml., bringing the total for region d to 815 ml.

My final estimate of the distribution of blood in the resting human body is accordingly as follows:

Region		P.C.	ml.
a	Heart, lungs, large vessels	40	1400
b	Liver	13	450
c	Skeletal muscles	24	850
d	Viscera (except liver) glands of head and neck, central nervous system, skin, skeleton, adipose tissues	23	800
	Total ml.		3500

It will be noted that the chief difference between this estimate and that generally quoted is in the greater proportion of blood assigned to the heart, lungs and larger vessels, and the markedly smaller proportion assigned to the liver.

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Pathogenesis and Prognosis of Angina Pectoris.

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ANGINA PECTORIS may be defined as a disease characterized by paroxysmal attacks of pain precipitated by emotional excitement or physical exertion, usually pectoral and associated with vascular changes. It is a definite clinical syndrome which must be clearly differentiated from coronary thrombosis and other forms of anginal pain not occurring in the characteristic syndrome. Many authors have failed to make this clear-cut distinction which has rendered their investigations less valuable than they might have been and handicapped us in arriving at a precise knowledge of the disease and its prognosis.

Predisposing Causes.

Age: Its maximal incidence is reached between the ages of 50 and 60, beyond which its incidence decreases. Cases under 30 and even 25, are not very uncommon.

Sex: 90-95 per cent. of cases are in men. This is related to the relative frequency of cardio-renal vascular diseases in the two sexes.

Race: The disease reaches its highest incidence in the United States and Canada. This is probably due to the relatively high pressure of living in these two countries. Jews are said by Osler to be especially prone, but it is very hard to sustain this fact in dealing with such a neurotic people.

Occupation: Angina Pectoris is the "worry disease of all nations." The high incidence amongst lawyers, doctors and business men is notorious.

Heredity: This factor is prominent, having as it has, such a close relationship to cardio-vascular disease.

Etiology and Pathology.

From the etiological standpoint Angina Pectoris may roughly be divided into two life periods, viz.: (1) where the onset is before 40-45 years of age, and (2) where it is after 40-45 years. Inflammatory changes are the basis of the first set of cases and degenerative changes of the second. The last group form by far the majority. The inflammatory group is infective and in order of incidence are (1) Rheumatic Fever, (2) Syphylis, (3) focal infections in general, teeth, tonsils, sinuses and so on. The most common finding in Angina Pectoris is coronary sclerosis with the usual picture of so-called "chronic myocarditis" which is actually merely a degeneration of muscle fibres and their replacement by fibrous tissue. This coronary sclerosis may or may not be part and parcel of a general arterio-sclerosis. Arterial hypertension is commonly found in the disease or preceding it. Angina Pectoris occurs most often in a predominating left ventricular failure, so that it has often been termed "failure with angina," though only some 50 per cent. have angina and some 30 per cent. of this true Angina Pectoris.

Coronary artery disease is present in 75-80 per cent. of all cases. Of the other common causes may be mentioned aortitis, valvular disease (especially aortic and of that aortic insufficiency), adherent pericarditis, aneurysm of the aorta, dilatation of the aorta. Not a few cases are mentioned in the literature in which there are no pathological findings at necropsy.

As many patients with coronary sclerosis and a seriously damaged myocardium suffer no pain, it is evident that some factor in addition must produce the syndrome of Angina Pectoris. The precise nature of this factor is unknown, but the following consideration of theories is worth while:

(1) Stevens maintains that this factor has to do with a hypersensitiveness of the central nervous system which is much more pronounced in some individuals than in others. He supports this with the observation of the frequency with which the disease attacks doctors, lawyers and actors, and the intellectually trained portion of the community. This incidence is much more easily explained upon the increased frequency of hypertension and arterio-sclerosis in this class.

(2) Some feel that the pain is due to a neuritis or neuralgia of the nerves or sym-

pathetic ganglia. Most notable among these is Lanceureaux and Peter, who attribute it to a neuritis of the cardiac plexus of nerves. In this connection work on the nerve paths leading to the suggestion of sympathectomy as treatment is of interest.

The entire cervical sympathetic system has been shown by Langley and Ranson to be purely efferent. The vagus would not be effective in causing pain referred to the chest, for the somatic afferent fibres of this system have no distribution in this region. While sympathectomy has given definite relief, in some 60-65 per cent. of cases, removal of the depressor (bulbo-sacral vagus) as suggested by Wenkebach, Eppinger and Einthoven, has led to no such result. Coffey and Brown have shown that extirpation of the superior cervical ganglion leads to the disappearance of pain. Thus this ganglion must be involved in the nervous arc, producing anginal pain, and since it contains only efferent fibres it must be on the motor side of the cycle. As Ranson points out, no matter what paths the stimulus follows, it ends in the first three or four dorsal roots. Head claims that the collar pain around the upper part of the neck over the jaw is due to a referrance from the vagus into the distribution of the upper cervical and trigeminal nerves.

(3) Heberden and later Latham ascribe the phenomenon to a cramp of the myocardium. This hypothesis is not well sustained.

(4) Traube, Lauder Brunton and others have attributed it to an overdistension of the ventricles. Albutt for many years has maintained that it is due to and produced by disease of the aorta, more especially of that part just above the sigmoid valves, and that the immediate cause is undue distension of the fibrous adventitia of the vessel.

(5) Allan Burns of Glasgow, in 1809, and later Potain, and more recently Osler, attribute it to a phenomenon analagous, if not identical to intermittent claudication, occurring in voluntary muscle. This hypothesis appears to be gaining ground of late.

Prognosis.

Few writers have had the courage to attempt anything like an exacting statement as to the outcome of this so uncertain of diseases. Sir James MacKenzie collected records of 380 cases which he saw and treated, but did not separate patients with typical coronary sclerosis. More recently White has added a series of 200 consecutive cases, of Angina Pectoris, seen in practice, to the literature.

All students from Heberden's time down to Osler, have felt the need of lightening the dire verdict of this disease. As Albutt points out, the prognosis is by no means invariably fatal. In MacKenzie's series of 213 cases the average duration from the onset to death was 5.4 years. In 284 cases he was able to trace death to myocardial failure in 213. In mentioning bad prognostic signs he draws attention particularly to pulsus alternans, nocturnal orthopnea, and Cheyne-Stokes respirations. Important, but by no means infallible, also is the ease with which an attack is provoked. Each case must be studied on its own merits in arriving at a reasonably accurate prognosis. The factors which must be valuated are occupation, age of onset, sex, presence of arterial hypertension, arterio-sclerosis and its extent, renal or other co-incident disease, enlargement of the heart, heart block, presence or absence of syphilis, character of the "T"-wave in the electro-cardiogram and the general stability of the patient's nervous system.

In 148 of White's cases examined by the electro-cardiogram 38 cases, or 26 per cent., showed normal hearts on physical examination, normal blood pressure and normal electro-cardiograms. Of these 38 cases 11, or 29 per cent., survived at least five years. Of the remaining 110 patients who showed abnormal hearts 34, or 31 per cent., died within five years. The average duration of the disease in White's statistics was 4.0 years. This is definitely lower than MacKenzie's figures. Addiction to alcohol and tobacco does not appear to affect the prognosis.

Conclusions.

(1) The underlying pathology of Angina Pectoris is even yet but poorly understood. The usual lesion is a sclerosis of the coronary vessels with a chronic myocarditis. The actual pain is probably most often due to a phenomenon akin to intermittent clau-

dication, though no cause is constant likely in all cases or even in the same case at all times.

(2) To arrive at a clear understanding of Angina Pectoris great care must be taken in excluding coronary thrombosis and anginal pain not belonging to the characteristic symptom complex of Angina Pectoris.

(3) In arriving at a reasonably accurate prognosis each case must be carefully investigated and judged upon its own merits.

(4) The prognosis in the disease is not so grave as was formerly believed.

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Hereditary Deforming Multiple Enchondromata.

AN INTERESTING HEREDITY STUDY.

K. E. FERRIE, 2T7.

THIS condition is an hereditary familial disease, accounts of which are quite rare in the American literature. A very interesting case of this disease appeared at the Hospital for Sick Children last February, and may be of interest to the readers of this journal. Although this condition has been commonly recognized in the European countries, especially in Germany, and has been reported in various articles under many different names in America, the literature is rather scant, as can be noted by Ehrenfried's review of the subject. In his article he mentions that he found only four case reports, however, more are now in print in America. The first case reported in America was by Gibney in 1875.

Nationality: Germans, 60 per cent.; French, 27 per cent.; English, 8 per cent., and all other countries 5 per cent.

Sex: 3 males to 1 female.

Heredity: The majority of cases reported are single cases and very few make mention of the heredity history which is available in this present case and appears in the accompanying table.

Etiology: The exact etiology of this condition is unknown, the literature tells us that it can be transmitted by an unaffected female or by an affected male. It is thought by some to be caused by rickets, endocrine disturbance, or trauma.

Pathology.

Multiple cartilagenous exostoses usually appear about the epiphyses in young people. They are often partly cartilaginous for a time, but in the end are bony. They sometimes interarticulate with one another, or, by fusing limit the motion of the joint or may dislocate it.

C. A. Hamann, in his article, states that the pathology of such a growth removed from a femur resembled a chondroma. "There is a thick limiting membrane at the

periosteum; under this there is a thick mass of cartilage, in which the lacunae are extremely numerous, somewhat irregular in size, but generally larger than normal. At a distance of about 1 mm. from the surface, there is a considerable deposit of calcium salts associated with extremely few osteoclasts and osteoblasts without lamella formation."

Occurrence.

This condition may be present at birth and noticed first in infancy, although it is usually recognized in childhood. The symptoms are noticed during the period of skeletal growth. The tumours themselves are usually not painful, but may interfere with the function of the part involved and in this way become painful.

X-Ray Findings.

The accompanying X-Ray shows a typical enchondroma just at the proximal end of the 1st phalanx of the 1st finger of the left hand, about the size of a marble, the deformity is also clearly shown.

Case Report.

Name: John Smith, age 10 years. Sex: male. Canadian.

Complaint: (1) Deformity of index finger left hand.
(2) Deformity of left foot.

Duration: 5 years.

Family History: Mother, father, 3 brothers, and 5 sisters alive and well. The father, who has been a victim of this disease and who has observed it in others for many years, states that in some cases where there have been tumors without deformity that the tumors entirely disappeared without leaving any sign of their erstwhile presence. For further family history see Chart.

Personal History: Patient has had measles, mumps, whooping cough and chicken pox. He has had no other illness.

Tumor

Present Illness: When about 5 years old the present deformity of the left index finger first became noticeable, gradually becoming more marked until one year ago. Since then no change has been noted.

The deformity on the sole of the left foot was not observed till one year ago; it has bothered him a little.

The lumps observed on the posterior aspect of the right hand have been present only for the past few months. These areas have never broken down, become infected, or tender. There is no pain associated with them.

His general health has always been good.

Physical Examination.

The child is a well-developed and well-nourished male, 10 years of age, is of good

intelligence and is normal in every respect except for his osseous system.

Special Examination.

Just at the proximal end of the 1st phalanx of the 1st finger of the left hand is a rounded swelling the size of a marble; it is intimately attached to the phalanx and moves with it. Movement of the joint is not painful. It has caused a deformity of the phalanx in that it is curved with its convexity towards the volar surface; this forms a marked depression on the dorsal aspect of the finger. The swelling is not tender, and it is very intimately attached to the bone and moves freely with it.

On the dorsal aspect of the 2nd and 3rd metacarpals near their distal ends there is a rounded swelling on either bone the size of a pea.

On the plantar aspect of the 4th left metatarsal bone there is a similar rounded swelling, a little smaller than a marble. It is situated near the distal end of the bone and intimately attached to it. Pressure over this causes pain, but the pain is apparently in the subcutaneous tissues.

A similar swelling the size of a marble was noted on the outer surface of the Right Radius, just proximal to the epiphyseal line.

Final Diagnosis.

Hereditary deforming multiple enchondromata.

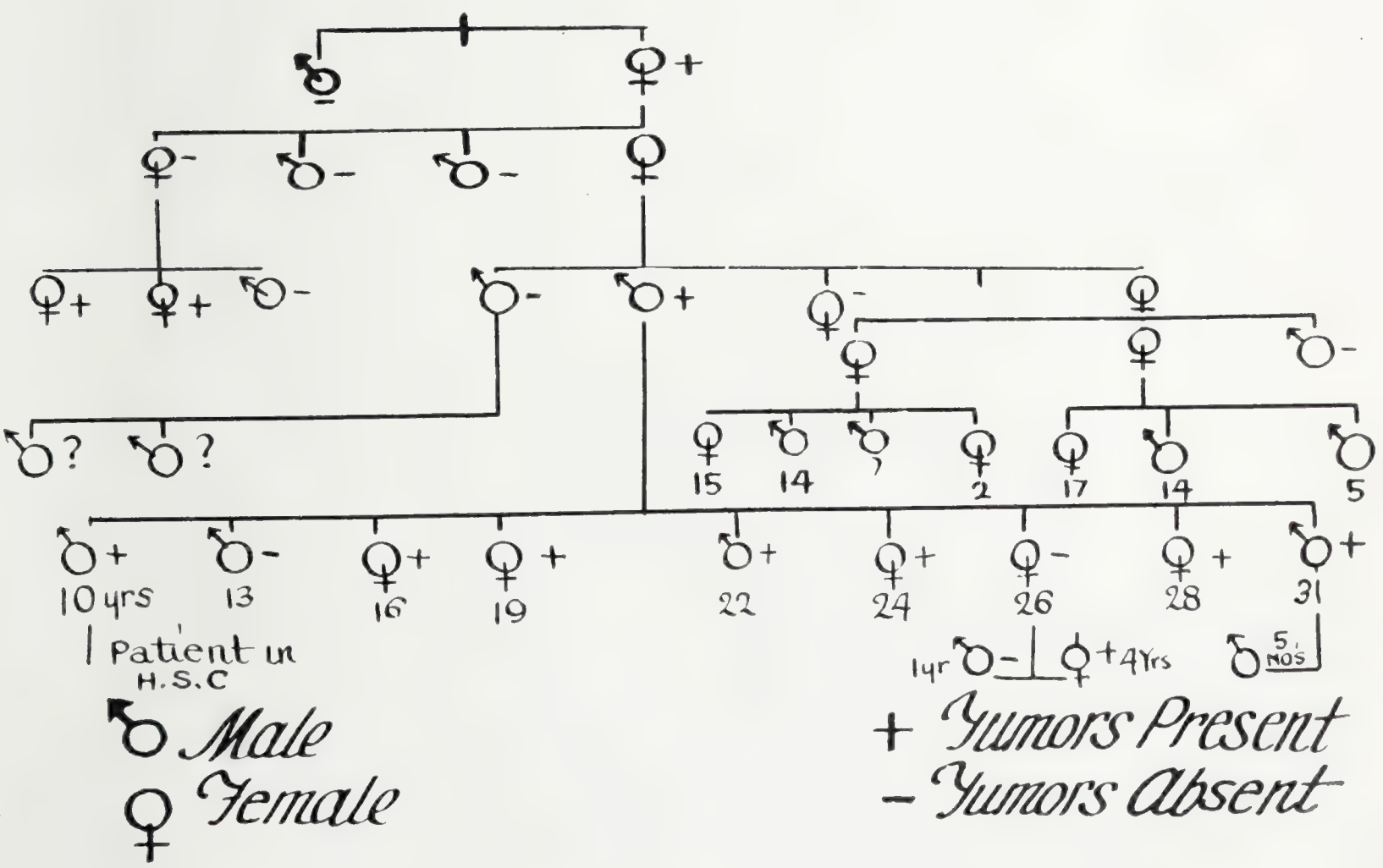
An operation was performed for excision of osteomata of the left index finger, right radius and left foot.

The tumours were removed showing normal bone underneath and were continuous with the shaft of the bone and the epiphysis. The epiphyses appeared to be considerably deformed, especially in the left index finger.

The indication for operation was the deformity, interference with function, and presence of tumor on pressure points.

Hereditary Factor in Enchondromata.

Ulrich describes multiple cartilaginous exostoses in a mother and daughter with an hereditary history. The basal metabolism was below normal in both cases and the blood calcium increased. He observed another case in a boy of a tuberculous family without any indications of heredity.



A study of 20 families in the literature revealed that 50.3 per cent. of the children had exostoses. They are thought to be caused by a single dominant hereditary factor. Possibly the more severe cases of exostoses are due to a predisposition to this affection combined with another predisposition to short stature and short limbs.

In the present case I have not found this last statement to apply. In a total of 36 members of this family 40 per cent. had history of tumors, with a proportion of 7 females to 5 males. A parent with exostoses and a healthy parent may have healthy children as well as children with exostoses and transmission is by unaffected female or affected male. It is also interesting to note that there is a history of some of these tumors having completely disappeared around the age of puberty.

Conclusion.

There is very little known of the true nature of this condition. On looking through the literature one finds that the terminology is very variable, names most commonly used are multiple cartilagenous or hereditary deforming chondrodysplasia. Other names used to describe this condition are, ossified diathesis, multiple cancellous exostoses, rachitiform enchondrosis, chondral dysplasia, multiple congenital osseochondromata, hereditary deforming multiple enchondromata.

Hereditary deforming multiple enchondromata can no longer be considered a rare affection in this country. The disease is a distinct clinical entity, whose manifestations are well defined. The work which has been done on its Pathology points definitely to a disturbance in the bone forming cartilage as the underlying cause. The hereditary nature of the disease which has been pretty well demonstrated, gives it an individuality and makes its investigation interesting. The disease should be given wider recognition and study, not only from its importance, but also because it opens up the whole field of obscure congenital skeletal affections.

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Recent Respiratory Stimulants.

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THE TYPE of case in which respiratory stimulant is indicated clinically is usually accompanied by some circulatory failure. Respiratory stimulants at best have only a somewhat evanescent effect, and therefore lend themselves to use only over short periods of time, where they can serve to tide the patient over the crisis of some sudden respiratory and circulatory depression until normal activity is again resumed.

Respiratory and circulatory depression which can be beneficially treated by such stimulants is usually caused by some toxin or poison acting on the centres and is well exemplified by morphine poisoning. In a well developed case the respirations are very slow, stertorous or frequently shallow; occasionally breathing of the Cheyne-Stokes type occurs. The pulse is slow and gradually becomes very weak and finally impalpable.

In other types of intoxications the respirations are very rapid and superficial and the pulse markedly accelerated, weak, thready, or even impalpable. The anaesthetics, chloroform, ether, and also the stronger hypnotics such as chloral hydrate, are only too prone to affect the heart and respirations unfavorably. Chloroform is, of course, the outstanding offender, but any of the anaesthetics or hypnotics when given in overdoses will produce similar results. In addition there must be mentioned all those substances frequently taken with suicidal intent, such as lighting gas, phenol, etc.

We do not here need to consider such therapeutic measures as the inhalation of CO_2, which affects only the respirations, nor of adrenalin and caffeine, whose primary action is on the circulation. The clinical effect of these substances is definite and well known.

Camphor has long held a clinical reputation as a stimulant in depression of the circulatory system or respiration, but the pharmacological evidence which has been adduced to support this claim has never been very satisfactory. Striking effects can be shown under certain conditions of experimental intoxication, but these have never seemed to justify the rather wide-spread clinical regard in which it has been held, particularly in Germany where it has been used in a wide variety of circulatory failures and also as a stimulant to the respiratory centre, particularly in cases of intoxication with morphine, the hypnotics and anaesthetics, or in the terminal stages of infectious diseases, particularly pneumonia. It cannot be said, on reviewing a large number of cases so treated, that the effects have been very striking or brilliant, and the results have been irregular, that is, under apparently similar conditions, differing results were produced. To a large extent the failures have been ascribed to the extremely low solubility of camphor (1/1000), and the impossibility therefore of getting it to the site where its effect was desired either sufficiently rapidly or in sufficient concentration. The consequence has been more active study in recent years of possible substitutes for camphor.

Isopropylcyclohexanone.---The first of these substitutes was suggested by Gottlieb and Schulemann. Chemical workers attempted to produce camphor derivatives which were readily soluble. The result of their efforts was the 3-isopropylcyclohexanone introduced under the trade name of hexetone. This substance is not very soluble in water but is readily soluble in a solution of sodium salicylate. It has now been very widely studied and quite frequently employed in German clinics, and I think one may fairly say that it has the following pharmacological effects. It seems to have no effect on impulse production in the heart and little effect on cardiac contractility (Stross). It seems to have no effect in auricular fibrillation but seems to somewhat decrease sinus arrythmia and the production of extrasystoles. When it has been used in pathological conditions it has been noted that unduly fast hearts somewhat decrease in rate in many cases, while those of normal rate sometimes increase by a few beats (Krehl and Franz). As far as the circulation is concerned, its chief effect seems to be on the vasomotor centre which is undoubtedly stimulated (Gottlieb and Schulemann, Stross, etc.). This makes it useful in cases of collapse and in cardiac inefficiency due to lack of vascular tonus such as occurs so frequently in pneumonia, or as a terminal effect in the cases of severe poisoning with such drugs as the hypnotics or even morphine. The respiratory centre is undoubtedly stimulated and respiration improved. This is particularly evident when the respiratory centre has been depressed with morphine or the hypnotics (above and Leschke), and in poisoning by lighting gas (Taschenberg). Its effects on a respiratory centre depressed by chloroform are not so great if one may judge from the evidence as yet presented.

Part of the effect of hexetone on the respiratory centre seems to be due to the sodium salicylate present. Thus Modrakowski and Sikorski found that a similar quantity of sodium salicylate had as much effect in increasing the respiratory rate as did the salicyate solution of hexetone. Helaers confirmed these results but in addition showed that respiratory volume was much more affected by hexetone than by salicylate alone. Also he showed that hexetone dissolved in sodium benzoate, the benzoate having no action on the respirations, consistently produced definite improvement in the respira-

tions. Thus we may conclude that hexetone itself acts as a respiratory stimulus, but that it is aided in this action by the sodium salicylate in which it is dissolved.

It has undoubtedly an effect on the cerebrum. Several observers have noted that the brain if confused or depressed becomes clearer (Krehl and Franz), and it is known that in larger doses in animals it produced convulsions which are of a cerebral type (Gottlieb). It may be given either intravenously 0.01 gms., or intramuscularly 0.2 gms., or in the same dose per os, and repeated every half to two hours in man, even for a day or two (Krehl and Franz). It should not be given subcutaneously or in an oedematous area or in a fatty tissue, as then irritation or even necrosis may supervene, probably due to the sodium salicylate (Rominger, Julich). In intravenous doses, if not very slowly administered, it is apt to produce a state of anxiety with various sensations such as waves of heat and cold with sweating, and in consequence its intravenous use is better avoided save in cases where it is urgently necessary (Senner). The maximum effect occurs at the end of some thirty minutes when given intramuscularly.

Hexamethylenetetrazol.—The second drug is one which departs very largely from the camphor constitution. It may be described chemically as hexamethylenetetrazol and has received the name of cardiazol (Schmidt, Hildebrandt, Krehl). This substance is readily soluble in water and in the usual solvents. Its watery solution can be sterilized and is neutral in reaction. On normal hearts it has little effect. If any occurs it consists in an increase in contractility with a decrease or no change in rate, and in various types of damage produced in isolated hearts, such as over-stretching of the auricle, prolonged perfusion, the administration of chloral, quinine, chloroform, or lack of calcium the effect is only on contractility (Stross). In many of these types of cases its effect is temporary and adrenalin and caffeine give better results. It appears to decrease the excessive cardiac irritability, as evidenced by abolishing extrasystoles produced by strophanthin (Schmidt, Hildebrandt, Krehl, etc.). In the intact animal it frequently decreases cardiac rate owing to a central vagus effect, especially if the rate is high. For the vastomotor centre it is the best known stimulant, surpassing strychnine, caffeine, atropine, and the other drugs mentioned in this paper. Its effect in raising blood pressure, when abnormally low ,is greater than any of these others, though not so prolonged apparently as that due to coramine. It has been reported to relieve the spasm in angina (Hemmerling). Its effect on the respiratory centre when depressed, is very marked. It seems to increase the depth rather than the rate of respiration, though both seem to be increased in some cases. It has also some cerebral effects and patients are brought out of a cerebral depression due to hypnotic drugs, morphine and anaesthesia, relatively rapidly (Ruef, Voss). It increases the depth of respiration soon after the ending of a long anaesthesia, increasing the ventilation of the less active parts of the lungs and in consequence it is believed to have decreased post-anaesthetic pneumonia. Its effects in morphine poisoning are very marked. This we have seen in various experiments performed in this laboratory. For instance, a rabbit of 2 kilos, whose respiration completely ceased with 28 mgm. of morphine and whose blood pressure had begun to fall owing to the accompanying asphyxia, was given 40 mgm. of cardiazol intravenously. This resulted in a prompt re-awakening of respirations at a relatively slow rate but gradually increasing depth which were maintained for a long period of time (half an hour) with an increase in blood pressure above normal and a marked increase in pulse pressure. The cardiac rate was decreased. This animal was then given 160 mgm. of morphine intravenously (over five times the previous dose which produced complete respiratory depression) yet this amount only decreased the rate of respiration and made it irregular with pauses, but for a period of another half hour this type of respiration continued with little or no failure in the blood pressure or pulse pressure. In another animal similar results were obtained and it was noted that the intravenous injection of a small amount of adrenalin led to a prolonged increase in pressure and also to a marked acceleration in respiratory rate with a corresponding decrease in depth which was also very prolonged. In dogs

when morphine is given in relatively large doses (10 mgm. per kilo.) the respiration is slow but deep, in this case the respiratory rate is increased and deepened by cardiazol and the animal awakes from his morphine sleep much more promptly. Cardiazol may be given subcutaneously 0.1 gm., or intravenously 0.05 gm., or per os, (Schmidt, Hildebrandt, Krehl). In children ¼ to ½ the adult dose may be given (Mertz and Eschbacher). These doses in an emergency may be repeated once or twice at half hour intervals and for long periods of time at two hour intervals.

In large doses cardiazol produces convulsions of a cerebral type in animals. This may also occur in decorticated animals and it re-awakes certain of the reflexes in deep narcosis (Schoen).

The diethylamide of pyridin-carboxylic acid, (diethylnicotinamide) departs even further from the camphor structure. It is a colourless, almost odourless fluid, neutral in reaction, and is put up in a 25 per cent. solution in water, under the name coramin. On normal hearts it produces no effects save in large doses, when it produces decrease in rate and stoppage, but the contractility and conductivity over the auriculoventricular bundle are not affected even by these toxic doses. When damage is produced artificially in isolated hearts by auricular over-distension, prolonged perfusion, lack of calcium, presence of chloral or quinine, it produces no improvement and is not to be compared to adrenalin or caffeine. On hearts poisoned with chloroform it has little or no effect (Strass). It has little effect on the vagus centre but stimulates the vasomotor centre giving an increase of blood pressure in poisoning by chloral and morphine, and in cases of post-operative low blood pressure or collapse of various origins. Also like cardiazol it improves the respirations after long prolonged anaesthesia. It also stimulates the cerebrum in animals in large doses as evidenced by an increase in activity and tendency to bite, and in further large doses causes convulsions also of cerebral type (Schubel, Uhlmann). Some observers have also noted that there is a marked improvement in the appetite of patients receiving this medicament (Hirsch). It may be given either per os, intravenously, or subcutaneously, in doses of 1-3 cc., two or three times per diem. It is quickly absorbed in all these types of administration. To children it may be given per os in milk (Hirsch). If repeated at the above frequency in animals there is no evidence of habituation being produced and in large doses there is, on the other hand, some evidence of increased susceptibility to its toxic effects, especially those on the heart in which it produces a systolic arrest (Schubel). It has been used by numerous workers but it has not been compared for its effects on respiration with other drugs. Nor does the literature as yet suggest that its action is as great as that of cardiazol, though it is perhaps a little more prolonged.

A-Lobeline.—This drug was the result of a more careful study of the alkaloids of lobelia by Wieland and Meyer. It is an undoubted stimulant of respiration but is very transitory in its action. If injected intravenously it may cause quite alarming preliminary symptoms, cessation of respiration lasting two or three minutes, nausea with vomiting, sweating, and bradicardia, decreased blood pressure and colic. These are probably due to a stimulation of the vagus centre. It does not seem in any dose to improve the cardiac action nor to increase the blood pressure. In these respects it does not compare favorably with the above mentioned drugs, and further, the clinical cases reported have abundantly illustrated the evanescent character of its stimulant respiratory effect and the alarming symptoms that sometimes accompany its use.

All these drugs are still under investigation but at present there is not sufficient clinical evidence to warrant all the profuse therapeutic claims set forth by their producers.

A Parodied Proverb From St. Barts' Med. Journal—"Voracity is the mother of indigestion."

Liver Damage.*

I.—PHYSIOLOGY OF BILE PIGMENTS

J. SHIER, 2T8

THE classification and study of the different clinical types of jaundice is so closely associated with the biochemistry of bilirubin that it seems advisable to review some of the chemistry relating to this substance.

The experimental facts indicate quite definitely that the source of bile pigment is hemoglobin. Bile pigment is merely iron free hemoglobin.

The site of transformation of the hemoglobin into bile pigment was for a long time considered to be the liver. The following evidence seems to prove conclusively that although the liver cell has considerable power in removing bile pigment from the plasma it does not elaborate it. In conditions such as acute yellow atrophy, phosphorus and chloroform poisoning where there is extensive damage to liver cells it is common knowledge that the more extensive the damage to the liver cell the more intense is the jaundice; which fact would not be expected if the liver cell was responsible for the production of bilirubin.

If the liver cell elaborated bile pigment and excreted it into the biliary passages one would not expect to find bile pigment in the blood. It is, however, present in blood. This latter fact seems to indicate that the bilirubin is formed elsewhere in the body and is carried to the liver by the circulating blood to be excreted there.

Inquiring further into the site of formation of bilirubin Mann and Rich working separately showed that in hepatectomized dogs bile pigment increased in the plasma in 3-6 hours and that the appearance of the pigment could be hastened by the injection of hemoglobin into the blood stream.

If the bile pigment can be produced outside of the liver is it produced extracellularly or intracellarly and if the latter what particular cell is responsible, or may any cell carry on this function? Since no enzyme, tissue extract or sterile tissue medium has been found which is capable of producing bile pigment we have nothing on which to base a belief that bilirubin may be formed extracellularly. For the time being we must believe that bile pigment is produced intracellularly. But this is not a function of all the cells of the body, for if a vein in a dog be ligated and hemolysis be brought about or hemoglobin introduced, no bile pigment is found within the vein, even after a considerable lapse of time. Thus it is seen that the ordinary endothelium of the blood-vessels does not elaborate bile pigment.

Lowit observed that in frogs in which extensive intravascular hemorrhage had taken place that the Kupffer cells of the liver sinusoids contained large quantities of fragmented erythrocytes, hemoglobin, bile pigment and iron. He found similar cells each containing similar material in the spleen, and bone marrow. He drew the conclusion from this observation that these special cells were responsible for the production of bile pigment.

Lowit's observation received rather scant attention and it was some years later that Aschoff, among other observers, described a type of cell, which although scattered rather widely throughout the animal body, had similar morphological and functional characteristics. To this group of cells he gave the name of reticulo-endothelial system. These cells were found in the liver, lining the sinusoids, in the spleen, lymph glands, bone marrow, connective tissue, adrenals, and circulating blood.

It was McNee, however, who broke away from the idea that the liver cell was responsible for bile pigment formation and who ascribed to the cells of the reticulo-endothelial system this particular function.

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* Delivered before the A.O.A. fraternity, March 1927. This subject is dealt with in two articles, the second of which, a clinical discussion, by Mr. H. Borsook, will appear in the May issue.

Such a theory as this of McNee's helps us to explain a number of points, as for instance:

1. Why the splenic vein contains more bile pigment than the splenic artery. The spleen, as stated above, is rich in these particular cells and these secrete bilirubin into the blood as it passes through this organ.

2. Perfusion of the spleen with laked blood leads to an increase in bile pigment in the perfusion fluid, whereas perfusion of another capillary bed such as the heart-lung preparation, results in no appreciable increase in bile pigment. The difference in these results may be accounted for by the fact that the spleen is exceedingly rich in reticulo-endothelial cells, whereas the heart-lung preparation is comparatively deficient in cells of this type.

3. The formation of bilirubin in extravasated blood is most likely due to the activity of these cells which are always present at the periphery of the blood mass.

4. There is no observation on record where bilirubin has been formed in the absence of cells of this particular type.

So far I have attempted to show that bilirubin derived from hemoglobin is not formed in the liver cells, nor in tissue fluids, but by cells of the reticulo-endothelial system which have a wide distribution throughout the body.

Next let us direct our attention to the chemistry of bilirubin. The chemistry of this substance is of particular interest to us in the interpretation of the two types of Van den Bergh reaction. The Van den Bergh reaction is based on Erlich's discovery of the fact that bilirubin has the power of combining with diazo compounds to form a purple dyestuff. Van den Bergh noticed that the bilirubin in bladder bile and in the sera of cases of obstructive jaundice combined immediately with the diazo reagent to form the purple dye-stuff, this is called the direct reaction. On the other hand bilirubin in normal serum and in cases of hemolytic jaundice reacted not at all, or only very slowly, to form the purple-pink compound, but the purple colour may be produced almost immediately by the addition of alcohol; this is called the indirect Van den Bergh.

Some proposed the theory that there were two types of bilirubin. In bladder bile and the serum of cases of obstructive jaundice they believed that the bilirubin was in free form and hence readily combined with the diazo reagent. In normal serum and in serum of cases of hemolytic jaundice they believed that the bilirubin was combined with protein and hence was not a suitable form to combine with the diazo reagent. However, if alcohol was added they believed the protein was precipitated and the bilirubin was liberated so that it could now immediately combine with the Van den Bergh diazo reagent to form the purple dyestuff.

Collison and Fowweather of the University of Leeds advance another theory in explanation of the Van den Bergh reactions. This theory is based on the physical and chemical properties of bilirubin and seems more reasonable than the above theory.

Bilirubin is an acid and hence forms salts. The salts are soluble in water, but insoluble in alcohol. The bilirubin of bladder bile and in the serum of obstructive jaundice is supposed to exist as salts, and hence forms true solutions in water and slightly alcoholic solutions and thus is in a state to react immediately with diazo reagent to produce the purple colour. On the other hand bilirubin of normal serum and in cases of hemolytic jaundice is in a free acid form and does not form a true solution in water, so that the reaction with the diazo reagent takes place slowly or, not at all, until alcohol is added. In this case the free bilirubin goes into solution and reacts immediately with the diazo compound and the purple colour is produced. This is the indirect reaction.

Thus we see that the bilirubin of the serum or normal individuals and cases of hemolytic jaundice is in the free acid form and does not form a true solution. The bile pigment in bladder bile and in serum of obstructive jaundice is in the form of salts, forming a solution. Lastly, the purpose of the alcohol is to put the free bile acid into solution, so that it may react readily with the Van den Bergh reagent.

Although the change of the free bilirubin of the serum to the salt form in the bile most probably takes place under normal condi-

tions in the liver, we must admit that passage through a liver cell is not necessary for this change and that the bilirubin may appear in salt form in the serum without ever having come in contact with a liver cell. From this we may conclude that the production of a direct Van den Bergh reaction does not necessarily mean that the bile pigment has passed through a liver cell.

Next, we may consider the amount of bile pigment present in normal serum. This is determined by means of the indirect Van den Bergh reaction which consists of adding to the serum, diazo reagent together with alcohol. The latter is added so that the free bile acid as well as salt will be in true solution to react to form the full depth of colour. The pink colour so produced is compared with a standard containing one part bilirubin or its equivalent in 200,000 parts of solution. A solution of this concentration is said to contain one Van den Bergh unit. By this method normal serum is found to contain from 0.2 to 0.5 units of bilirubin, that is from one part of bilirubin in 1,000,000 of solution to one part in 400,000 of solution.

When now an excessive amount of bile pigment appears in the blood so that the tissues become stained and bile pigment is excreted in the urine, the condition is known as jaundice. The concentration of bilirubin in the serum when clinical jaundice manifests itself is usually about 4 units of the Van den Bergh reaction. When the concentration of bile pigment is above 0.2-0.5 units, but yet is not high enough to clinically manifest itself, in other words it has not reached the concentration of 4 units, a state of latent jaundice is said to exist. This condition, from a clinical point of view, is of greater interest than true clinical jaundice, since it is an early indication of damage to the biliary mechanism and hence is a time when one would expect therapeutic measures to be more efficacious.

The increase in bile pigment in the blood over and above that which is normally present may be due to factors acting within the liver producing a hepatogenous jaundice or factors acting outside the liver producing a hematogenous jaundice.

Of the factors producing a hematogenous jaundice there may be an increased destruction of red blood cells, such as occurs in pernicious anemia with a resultant increased activity on the part of the reticulo-endothelial system, or there may be a primary increased activity of the reticulo-endothelial system such as may be the case in hemolytic icterus, with a resultant increased destruction of red cells. In either case the excessive amount of bile pigment is carried by the circulation to a more or less normal liver cell in greater quantities than it is capable of excreting, and as a result the bile pigment steadily increases in the circulating blood until we have the hemolytic type of jaundice produced.

Of the factors acting within the liver causing jaundice we may first consider blockage of the biliary passages. This may be due to a foreign body in the lumen of a duct, such as a stone, to something arising from the wall of the duct as a papilloma or something pressing on the duct from without and occluding its lumen, such as an enlarged lymph gland. The bile in the ducts is supposed to increase in quantity and pressure and eventually find its way into the circulating blood accumulating there until jaundice of the obstructive type is produced. The primary cause of jaundice here is the obstruction but whether the obstruction causes a reflux of bile into the blood stream again or merely alters the function of the liver cell through the pressure of retained secretions so that bile is not removed from the circulating blood I am not prepared to say.. The securing of a direct Van den Bergh reaction, as stated above, does not of necessity mean that the bile pigment has passed through the liver cell.

Lastly the other factor acting within the liver which may produce jaundice is a damaged liver cell. As a result of the impaired function of the liver cell the bilirubin is not removed from the circulating blood as it passes through the liver sinusoids and hence it passes on to the central vein and systemic circulation to accumulate there. This is the toxic and infective type of jaundice. The toxins and infective agents causing this damage to the liver cells may be put into five general groups:

(1) Chemical—as phosphorus, chloroform, and arsenic.

(2) Bacterial—as typhoid, pneumonia.

(3) Protozoan — as the spirochaete of syphilis.

(4) Auto-intoxicants—as uremia.

(5) Toxins of unknown origin—as eclampsia.

The pathology of the liver cell in toxic jaundice varies considerably from that which is difficult to demonstrate under the microscope but which is known to be present according to liver function tests, to cloudy swelling, fatty degeneration, partial and complete necrosis. Still more variable is the form of obstruction which is supposed to occur in this type of jaundice. Some, as Meutengracht, deny that there is any obstruction, and in looking over the references on the subject I could not find anyone who had definitely proved that there was obstruction. Others as Eppinger believe there is obstruction of finer bile capillaries due partly to the oedema of the cells and partly to inspissated bile forming mucous plugs. Other theories advanced in the past but now disbelieved have been; oedema of the head of the pancreas resulting in pressure on the common bile duct; oedema of the duodenum causing a closure of the ampulla of vater; or a mucous plug in the lower end of the common bile duct.

Although these three clinical groups of jaundice are named according to the primary factors causing each, one must admit that there are secondary factors contributing in a lesser degree to the production of the jaundice. For instance one cannot believe that in the hemolytic group some damage has not also been done to the liver cell either by the agent which may be responsible for the hemolysis or merely as a result of the poor hemoglobin content of the blood which normally keeps the cells in health by supplying oxygen and maintaining the body Ph. by its $C0_2$ carrying power.

Likewise in the obstructive group the retained secretions must have a toxic effect on the liver cell and possibly the constituents of the bile when they gain entrance into the blood stream have a hemolytic effect, as for example the bile acids.

Finally the toxin which causes the alteration in the liver cell would likewise have a deleterious effect on red cells causing their destruction.

Thus it is seen that although the term toxic jaundice is applied to that type of jaundice caused by the five groups of agents mentioned above nevertheless there is a toxic element existing in both the hemolytic and obstructive types.

Let us now consider the Van den Bergh reaction in the different types of jaundice. In pure hemolytic jaundice an indirect reaction is always secured; in the quantitative Van den Bergh the concentration of bile pigment in the serum is sometimes as high as twelve units and some have been reported as high as twenty units.

In obstructive jaundice a direct reaction is usually secured although early and late in the condition an indirect reaction is often reported. The concentration of bile pigment may reach the high level of eighty units.

In toxic and infective jaundice the Van den Bergh may be direct or indirect. It is often indirect until a unitage of four is obtained then the direct reaction is secured.

Thus it is seen that although the degree of jaundice may be determined fairly accurately by the Van den Bergh the results must be used rather cautiously in determining the type of jaundice. That is one must not try to diagnose the type of jaundice from the laboratory findings without taking into consideration the clinical evidence.

The concentration of bile pigment in the serum which must be present before biliuria occurs varies in the different types of jaundice. For instance the indirect Van den Bergh of obstructive jaundice is usually above four units before biliuria occurs, whereas in hemolytic jaundice it may be as high as twelve units. The difference in the concentrations four and twelve which is often obtained before biliuria is present may be due to the fact that in hepatic jaundice the bile pigment is present as a salt and is in true solution and hence can readily pass through the kidney filter. On the other hand the bilirubin in hemolytic jaundice is possibly present as free acid and this in water does not form a true solution and hence is not in a condition to pass through the kidney filter.

Report of a Case of Tetanus.

W. J. B. DERBYSHIRE, M.B.

ON SEPTEMBER 12th, 1926, a country girl of eleven years was brought to the Warren Hospital, Phillipsburg, N.J., suffering from severe pains in legs, back and neck. She had been treated at home for rheumatism for four or five days, but had gradually become worse. The child screamed with pain on being moved to her bed and had convulsions every few minutes. The parents could not give any history of injury.

On examination, opisthotonos and risus sardonicus were pronounced. The teeth were bared. Sordes were present and the breath was foul. The pupils were widely dilated and failed to react to light. On the legs were many small scratches and enlarged inguinal glands were palpated on both sides. The slightest external stimulus induced a painful spasm of the partially-contracted musculature during which dyspnoea and involuntary micturition occurred. Perspiration was profuse. The temperature by axilla was 101.4F and the pulse was 120 and regular. The girl was conscious and was, with difficulty, able to tell how she had scratched her legs whilst picking berries almost three weeks previous to admission.

As soon as the diagnosis was established, the patient was isolated in a quiet room and all the available tetanus anti-toxin serum—9,000 units, was given. An unsuccessful attempt was made to give the serum intraspinally, failure being due to the extreme opisthotonus. The subcutaneous route was then chosen. The patient complained of extreme thirst and liquids were administered freely as enemata of 10 per cent solutions of glucose and sips of sugared ice water and milk. At one time the child became markedly cyanosed due to the giving of a drink too rapidly and she was revived by artificial respiration.

At 7 p.m. on day of admission, more anti-toxin was obtained and 30,000 units of the concentrated serum were given intravenously. Save for a slight rise in the temperature no untoward symptoms could be attributed to the injection. To control the spasm a chemically pure 5 per cent, solution of magnesium sulphate was given subcutaneously in 10 ccs. doses every five hours.

The condition of the girl on the second day appeared better and although the temperature remained the same, the pulse was not so fast. At 11 a.m. 30,000 units of anti-toxin were given intravenously. Although the child cried with pains in legs and back, the spasms did not seem so violent and she was able to take egg-nogs and milk with lactose added. That night 30,000 units of anti-toxin were given intravenously and 20,000 units subcutaneously and the night report read that the child had not been so restless and that her condition seemed better.

During the third day the patient was able to take nourishment hourly between clenched teeth and without causing the spasms that had attended previous feedings. The general condition was much better although pain persisted and urination and defecation were still involuntary. The temperature had remained about 101F axillary until the morning of September 16th, the fourth day, when it dropped a degree and a half. The improvement in the patient continued and the last of the anti-toxin—20,000 units was given intravenously. Sodium Bromide, in 20 gr. doses, was given twice nightly during the following week as a sedative.

The girl got steadily better. Gradually the muscular spasms and rigidity subsided until on the 19th inst. (the seventh day) the patient voided voluntarily. Albumin was found in the urine.

A fortnight after admission the patient was put on full diet and was able to reach her mouth. Potassium iodide was given in dosage of minims five t.i.d. of the saturated solution, increasing it one drop a day in order to aid in clearing up the rigidity of the muscles.

Recovery was uneventful and the patient was discharged a month from the day of admission, showing only a slight stiffness of the leg and neck muscles and some retraction of the head to one side. A slight degree of torticollis was still present several weeks after her discharge although she was well otherwise.

The method used in treating this case was taken from that outlined in the editorial of the U. of T. Medical Journal of March, 1926.